

Application No. 09/678,202
April 7, 2004
Reply to Office Action of October 7, 2003

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application. Claims 1, 28, 29 and 31 have been amended as indicated below. Claim 27 has been cancelled without prejudice and without disclaimer of the subject matter thereof. Finally, new Claims 375-381 have been added.

Listing of Claims

1. (currently amended) A method of reducing the damage done by reactive oxygen species (ROS) in an animal comprising administering to the animal an effective amount of a metal-binding peptide which does not have a metal ion bound to it, the sequence of the peptide being having the formula:

$P_1 - P_2,$

wherein:

P_1 is:

$Xaa_1 Xaa_2 His[:]$ or

$Xaa_1 Xaa_2 His Xaa_3;$

P_2 is $(Xaa_4)_n$;

Xaa_1 is the N-terminal amino acid of the peptide and is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α -hydroxymethylserine;

Xaa_2 is glycine, alanine, β -alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α -hydroxymethylserine;

Xaa_3 is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

Xaa_4 is any amino acid; and

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n is 0-100;

or a physiologically-acceptable salt thereof.

2. (original) The method of Claim 1 wherein Xaa₁ is aspartic acid, glutamic acid, arginine, or α -hydroxymethylserine.

3. (original) The method of Claim 1 wherein Xaa₂ is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or α -hydroxymethylserine.

4. (original) The method of Claim 1 wherein Xaa₃ is lysine.

5. (original) The method of Claim 1 wherein Xaa₁ is aspartic acid, glutamic acid, arginine, or α -hydroxymethylserine, Xaa₂ is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or α -hydroxymethylserine, and Xaa₃ is lysine.

6. (original) The method of Claim 5 wherein Xaa₁ is aspartic acid or glutamic acid and Xaa₂ is alanine, glycine, valine, threonine, serine, or α -hydroxymethylserine.

7. (original) The method of Claim 6 wherein Xaa₂ is alanine, threonine or α -hydroxymethylserine.

8. (original) The method of Claim 7 wherein Xaa₁ is aspartic acid and Xaa₂ is alanine.

9. (original) The method of Claim 1 wherein n is 0-10.

10. (original) The method of Claims 9 wherein n is 0-5.

11. (original) The method of Claim 10 wherein n is 0.

12. (withdrawn) The method of Claim 1 wherein P₂ comprises a metal-binding sequence.

13. (withdrawn) The method of Claim 12 wherein P₂ comprises one of the following sequences: (Xaa₄)_m Xaa₃ His Xaa₂ Xaa₅,

(Xaa₄)_m His Xaa₂ Xaa₅,

(Xaa₄)_m Xaa₅ Xaa₂ His Xaa₃, or

(Xaa₄)_m Xaa₅ Xaa₂ His,

wherein Xaa₅ is an amino acid having a free side-chain -NH₂ and m is 0-5.

14. (withdrawn) The method of Claim 13 wherein Xaa₅ is Orn or Lys.

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15. (withdrawn) The method of Claim 1 wherein at least one of the amino acids of P₁ other than β-alanine is a D-amino acid.

16. (withdrawn) The method of Claim 15 wherein Xaa₁ is a D-amino acid, His is a D-amino acid, or both Xaa₁ and His are D-amino acids..

17 (withdrawn) The method of Claim 16 wherein all of the amino acids of P₁ other than β-alanine are D-amino acids.

18. (withdrawn) The method of Claim 15 wherein at least 50% of the amino acids of P₂ are D-amino acids.

19. (withdrawn) The method of Claim 16 wherein at least 50% of the amino acids of P₂ are D-amino acids.

20. (withdrawn) The method of Claim 17 wherein at least 50% of the amino acids of P₂ are D-amino acids.

21. (original) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because of the need to reperfuse an ischemic tissue or organ of the animal.

22. (original) The method of Claim 21 wherein the animal is suffering from cerebrovascular ischemia and the ischemic tissue is located in the brain of the animal.

23. (original) The method of Claim 21 wherein the animal is suffering from cardiovascular ischemia and the ischemic tissue is located in the heart of the animal.

24. (original) The method of Claim 21 wherein the peptide is administered prior to reperfusion, simultaneously with reperfusion, after reperfusion, or combinations thereof.

25. (original) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because of neurological trauma.

26. (original) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from a neurodegenerative disease.

Claim 27 (canceled)

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28. (currently amended) The method of any one of Claims 1-20 ~~Claim 27~~ wherein the peptide is administered to an animal exhibiting symptoms of possible cerebrovascular ischemia or possible cardiovascular ischemia while the animal is being diagnosed.

29. (currently amended) The method of any one of Claims 1-20 ~~Claim 27~~ wherein the peptide is administered to an animal prior to surgery, during surgery, after surgery, or combinations thereof.

30. (original) The method of Claim 29 wherein the surgery is open-heart surgery or surgery to transplant an organ into the animal.

31. (currently amended) The method of any one of Claims 1-20 ~~Claim 27~~ wherein the peptide is administered to an animal prior to radiation therapy, during radiation therapy, after radiation therapy, or combinations thereof.

Claims 32 - 374 (canceled)

375. (new) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from ischemia.

376. (new) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from ischemia of the central nervous system.

377. (new) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from a stroke.

378. (new) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from cardiovascular ischemia.

379. (new) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from myocardial ischemia.

380. (new) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from acute myocardial infarction.

381. (new) The method of any one of Claims 1-20 wherein the animal is in need of the peptide because it is suffering from angina pectoris.